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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/881,823	06/15/2001	Wenyuan Shi	22851-032	8957

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GRAY CARY WARE & FREIDENRICH LLP
153 TOWNSEND
SUITE 800
SAN FRANCISCO, CA 94107

EXAMINER
ZEMAN, ROBERT A

ART UNIT	PAPER NUMBER
1645	13

DATE MAILED: 06/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/881,823	SHI ET AL.	
	Examiner	Art Unit	
	Robert A. Zeman	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5-8,11-14 and 18-53* is/are pending in the application.

4a) Of the above claim(s) *5-8,11-14 and 18-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25-53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 7 .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

DETAILED ACTION

The amendment filed on 3-18-2003 is acknowledged. Claims 1-4, 9-10 and 15-17 have been canceled. Claims 25-53 have been added.

Election/Restrictions

Applicant's election with traverse of Group I in Paper No. 11 is acknowledged. The traversal is on the ground(s) that Groups I, II, VII and VIII are drawn to a monoclonal antibody related to the monoclonal antibody produced by the hybridoma deposited with the American Type Culture Collection as ATTC No. HB12559 and designated SWLA1. Applicant's arguments have been fully considered and deemed persuasive. Consequently, Groups I, II, VII and VIII are rejoined. Claims 5-8, 11-14 and 18-53 are pending. Claims 5-8, 11-14 and 18-24 are withdrawn from consideration. Claims 25-53 are currently under examination.

Information Disclosure Statement

The Information Disclosure Statement filed on 5-28-2002 is acknowledged. An initialed copy is attached hereto.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 25, 35 and 37-38 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 4, 7, 10, 12 and 17 of copending Application No. 09/378,577. Although the conflicting claims are not identical, they are not patentably distinct from each other because all claims are drawn to a method of treating or preventing dental caries comprising administering to a subject a chimeric monoclonal antibody wherein the chimeric antibody specifically binds to a cariogenic organism associated with dental caries and elicits a humoral immune response to an antigen displayed by the cariogenic organism and wherein the portion of said antibody that binds to said cariogenic organisms is derived from a species other than that of the treated subject.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Objections

Claims 28 and 43 are objected to because of the following informalities: the punctuation used to delineate the various deposited materials is confusing. It is unclear whether the 1), 2) and 3) are part of the deposit numbers. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 28 and 43 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that the hybridomas represented by the ATCC accession numbers, HB12559, HB112560 and HB12258 are required in order to practice the invention. The deposit of biological organisms is considered by the Examiner to be necessary for the enablement of the current invention (see 37 CRF 1.808(a)). The examiner acknowledges the deposit of organisms under the ATCC accession numbers HB12559, HB112560 and HB12258 in partial compliance with this requirement. However, said deposits are not in full compliance with 37 CFR 1.803-1.809.

If the deposit is made under terms of the Budapest Treaty, then an affidavit or declaration by Applicants or person(s) associated with the patent owner (assignee) who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty *and* that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 CFR 1.808.

If a deposit is not made under the terms of the Budapest Treaty, then an affidavit, or declaration by Applicants or person(s) associated with the patent owner (assignee) who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the following criteria have been met:

1) during the pendency of the application, access to the deposit will be afforded to one determined by the Commissioner to be entitled thereto;

2) all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent; and

3) the deposits will be maintained for a term of at least thirty (30) years from the date of the deposit or for the enforceable life of the patent or for a period of at least five (5) years after the most recent request for the furnishing of a sample of the deposited material, whichever is longest; and

4) a viability statement in accordance with the provisions of 37 CFR 1.807; and

5) the deposit will be replaced should it become necessary due to inviability,

contamination or loss of capability to function in the manner described in the specification.

In addition, the identifying information set forth in 37 CRF 1.809(d) should be added to the specification. See 37 CFR 1.803 – 1.809 for additional explanation of these requirements.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 25-53 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 25 is rendered vague and indefinite by the use of the phrase "an antigen displayed from by the cariogenic organism from the subject". It is unclear whether the antigen is from the cariogenic organism or the subject.

Claim 25 is rendered vague and indefinite by the use of the phrase "derived from a species other than that of the subject in need of such treatment". It is unclear whether said phrase refers to the subject to which the chimeric antibody is administered or any species which might need

such a treatment (i.e. all species susceptible to dental caries). If the former is true, it is suggested that the phrase "derived from a species other than that of the treated subject" be used.

Claims 28 and 43 are rendered vague and indefinite in that they recite non-elected inventions. Specifically, the instant claims are limited to antibodies with the CDRs of SWLA1.

Claims 29, 31, 44 and 46 are rendered vague and indefinite by the use of the phrase "includes an amino sequence of SEQ ID NO: X". It is unclear whether said phrase is referring to a portion of the recited SEQ ID NO or the whole sequence represented by said SEQ ID NO. Moreover, it is unclear whether said phrase is meant to convey open or closed claim language.

Claim 40 is rendered vague and indefinite by the use of the phrase "derived from a species other than that of the subject that hosts the cariogenic organism". It is unclear whether said phrase refers to the subject to which the chimeric antibody is to be administered or any species is capable of hosting the cariogenic organism. If the former is true, it is suggested that the phrase "derived from a species other than that of the subject to be treated with said monoclonal antibody" be used.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 25-35, 37-50 and 52-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shi et al. (Hybridoma Volume 17 No. 4, 1998, pages 365-371 – IDS-7) in view of Carter et al. (WO 92/22653).

Shi et al. disclose monoclonal antibodies with a binding specificity for the cariogenic organism *Streptococcus mutans*. Said antibodies include the IgG monoclonal antibody SWLA1. Shi et al. also disclose that said antibodies may have "great impact on future basic and clinical studies and the diagnosis and **treatment** of human dental caries. Shi et al. differs from the claimed invention in that their monoclonal antibodies are murine antibodies. Moreover, Shi et al. do not explicitly disclose that their SWLA1 antibody contains SEQ ID NO:1-4 ~~not~~ nor do they disclose that their SWLA1 monoclonal antibody contains the same CDR as the SWLA1 antibody produced by the hybridoma with the ATCC No. HB12559. However, it should be noted that, in absence of evidence to the contrary, the SWLA1 monoclonal antibody disclosed by Shi et al. is deemed to be identical to the SWLA1 produced by the hybridoma with ATCC and designated HB12559 and would contain the sequences recited in the rejected claims. Carter et al. disclose methods for the production of chimeric

antibodies where the specific binding domains are derived from murine antibodies and are used to replace the corresponding regions in human antibodies. Said human antibodies can be from any class of immunoglobulin and any isotype including IgG1, IgG2, IgG3 and IgG4 (see page 11, lines 11-18 of the Carter et al. reference). Moreover, Carter et al. disclose that the selection of particular constant domains to optimize desired effector functions is within the ordinary skill in the art. It also should be noted that humanizing antibodies is a standard procedure used in most immunology laboratories and therefore, it would have been obvious to one of skill in the art at the time the invention was made to use the methods of Carter et al. to "humanize" the murine antibodies disclosed by Shi et al. This "humanizing" consists of replacing the corresponding domains of the human antibodies of Carter et al. with the murine binding domains (light chain and or heavy chain CDRs) sequences of Shi et al. Given Shi et al. disclose that the SWLA1 monoclonal antibody would be useful in the treatment of dental caries coupled with the fact that Carter et al. state that chimeric monoclonal antibodies are less antigenic to humans and hence more effective therapeutically (see page 2-3 and page 5, lines 11-17), one would been motivated to humanize the SWLA1 antibody disclosed by Shi et al. using the methods disclosed by Carter et al. and to use the resulting chimeric antibody to treat dental caries. One would have a high expectation of success in making the required antibodies and using them to treat or prevent dental caries since Shi et al. disclose that the murine SWLA1 monoclonal would be useful in such a method and that the humanization of a given antibody reduces the deleterious antigenic responses associated with the use of murine antibodies in humans.

Claims 25-27, 33-42 and 48-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ma et al. (European Journal of Immunology 1994 Vol. 24 (1) pages 131-138) in view of Adair et al (U.S. Patent 5,877,293).

Ma et al. disclose methods for the production of chimeric monoclonal antibodies against *Staphylococcus mutans* in transgenic tobacco plants to be used in the treatment of dental caries in humans and other mammals (see page 131, second paragraph). The disclosed methods include: the cloning of heavy and light chain genes (see page 132); plant transformation and regeneration (see page 132); antibody chain detection (see pages 132-133); and measurement of chimeric antibodies and their binding capacities (see pages 133-134). Ma et al. differs from the claimed inventions in that both the heavy and light chains of the chimeric monoclonal antibodies are derived from murine antibodies. However, Adair et al. disclose methods for the production of chimeric antibodies where the light chains are derived from murine antibodies and the heavy chains are derived from human antibodies. Consequently, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the methods of Adair et al. to "humanize" the chimeric antibodies disclosed in the methods of Ma et al. This "humanizing" consists of replacing the murine heavy chain sequences of Ma et al. with the human heavy chain sequences of Adair et al. in the expression vectors of Ma et al. It should be noted that humanizing antibodies is a standard procedure used in most immunology laboratories. That, coupled with the fact that Ma et al. suggests "incorporating other regions such as the complement binding region of human IgG" (see page 137, second paragraph) and Adair et al. state that chimeric monoclonal antibodies are less antigenic to humans and hence more effective therapeutically (see column 1

lines 52-65), one would have a high expectation of success in making the required antibodies and using them to treat or prevent dental caries.

Claims 25-27, 33-42 and 48-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ma et al. (European Journal of Immunology 1994 Vol. 24 (1) pages 131-138) in view of Carter et al. (WO 92/22653).

Ma et al. disclose methods for the production of chimeric monoclonal antibodies against *Staphylococcus mutans* in transgenic tobacco plants to be used in the treatment of dental caries in humans and other mammals (see page 131, second paragraph). The disclosed methods include: the cloning of heavy and light chain genes (see page 132); plant transformation and regeneration (see page 132); antibody chain detection (see pages 132-133); and measurement of chimeric antibodies and their binding capacities (see pages 133-134). Ma et al. differs from the claimed inventions in that both the heavy and light chains of the chimeric monoclonal antibodies are derived from murine antibodies. However, Carter et al. disclose methods for the production of chimeric antibodies where the light chains are derived from murine antibodies and the heavy chains are derived from human antibodies. Consequently, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the methods of Carter et al. to "humanize" the chimeric antibodies disclosed in the methods of Ma et al. This "humanizing" consists of replacing the murine heavy chain sequences of Ma et al. with the human heavy chain sequences of Carter et al. in the expression vectors of Ma et al. It should be noted that

humanizing antibodies is a standard procedure used in most immunology laboratories. That, coupled with the fact that Ma et al. suggests "incorporating other regions such as the complement binding region of human IgG" (see page 137, second paragraph) and Carter et al. state that chimeric monoclonal antibodies are less antigenic to humans and hence more effective therapeutically (see page 2-3 and page 5, lines 11-17), one would have a high expectation of success in making the required antibodies and using them to treat or prevent dental caries.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A. Zeman whose telephone number is (703) 308-7991. The examiner can normally be reached on Monday- Thursday, 7am -5:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (703) 308-3909. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Robert A. Zeman
May 29, 2003

LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600